Complete Summary

GUIDELINE TITLE

Preventive health care, 2000 update: screening and management of hyperhomocysteinemia for the prevention of coronary artery disease events.

BIBLIOGRAPHIC SOURCE(S)

Booth GL, Wang EE. Preventive health care, 2000 update: screening and management of hyperhomocysteinemia for the prevention of coronary artery disease events. Canadian Task Force on Preventive Health Care. CMAJ 2000 Jul 11;163(1):21-9. [107 references]

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

- Hyperhomocysteinemia
- Coronary artery disease

GUIDELINE CATEGORY

Management
Prevention
Screening
Treatment

CLINICAL SPECIALTY

Cardiology
Family Practice
Internal Medicine
Nursing

INTENDED USERS

Advanced Practice Nurses
Nurses
Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

To establish guidelines for the screening and treatment of hyperhomocysteinemia in the investigation and management of coronary artery disease.

TARGET POPULATION

General population

INTERVENTIONS AND PRACTICES CONSIDERED

Screening

1. Screening for serum homocysteine in patients who have either no symptoms of coronary artery disease at baseline (primary prevention) or those with known coronary artery disease (secondary prevention).
2. Measurement of plasma total homocysteine levels (most commonly through the use of high-pressure liquid chromotography) in the fasting state or 4 to 6 hours after oral methionine load.

Prevention/Treatment

1. Vitamin supplementation with folic acid and vitamins B_6 and B_{12}.
2. Adherence to the recommended daily allowance of dietary sources of folate and vitamins B_6 and B_{12}.

MAJOR OUTCOMES CONSIDERED

- Total homocysteine levels and the risk of coronary artery disease (odds ratios and relative risk).
- Association between vitamin supplementation and total homocysteine levels.
- Cardiovascular death and overall mortality in patients with established coronary artery disease.

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The guideline developers conducted a computerized search of MEDLINE (U.S. National Library of Medicine) for English-language articles published between January 1966 and June 1999 using the MeSH (medical subject headings) terms "homocysteine," "hyperhomocysteinemia," "methionine," "coronary disease," "arteriosclerosis," "myocardial ischemia," "folic acid," "vitamin B_{12}," "vitamin B_6," and "pyridoxine" in various combinations. Relevant articles were also identified through a manual review of references. Where possible, the highest level of evidence was sought; hence, abstracts, cross-sectional studies, case reports and case series were not included. Studies concerning other types of vascular disease were also excluded.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Quality of evidence was rated according to 5 levels:

I - Evidence from at least 1 properly randomized controlled trial.

II-1 - Evidence from well-designed controlled trials without randomization.

II-2 - Evidence from well-designed cohort or case-control analytic studies, preferably from more than 1 centre or research group.

II-3 - Evidence from comparisons between times or places with or without the intervention. Dramatic results in uncontrolled experiments could also be included here.

III - Opinions of respected authorities, based on clinical experience, descriptive studies or reports of expert committees.

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

The task force, comprised of expert clinicians and methodologists from a variety of medical specialties, used a standardized evidence-based method for evaluating the effectiveness of this intervention. The final recommendations were arrived at unanimously by an expert panel and principal author.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Grades of Recommendation:

A. Good evidence to support the recommendation that the condition or maneuver be specifically considered in a periodic health examination.
B. Fair evidence to support the recommendation that the condition or maneuver be specifically considered in a periodic health examination.
C. Insufficient evidence regarding inclusion or exclusion of the condition or maneuver in a periodic health examination, but recommendations may be made on other grounds.
D. Fair evidence to support the recommendation that the condition or maneuver be specifically excluded from a periodic health examination.
E. Good evidence to support the recommendation that the condition or maneuver be specifically excluded from a periodic health examination.

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Comparison with Guidelines from Other Groups
External Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

The findings of this analysis were reviewed through an iterative process by the members of the Canadian Task Force on Preventive Health Care. Feedback from 2 content experts was incorporated into a final draft of the manuscript before submission for publication. The manuscript was then peer reviewed as part of the journal publication process.

Guidelines from the American Heart Association state that it may be reasonable to screen total homocysteine levels in people who are at risk for hyperhomocysteinemia or in those who have a personal or family history of premature atherosclerosis.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Recommendation grades [A, B, C, D, E] and levels of evidence [I, II-1, II-2, II-3, III] are indicated after each recommendation. Definitions for these grades and levels are repeated following the recommendations.

- There is insufficient evidence to recommend for or against screening for hyperhomocysteinemia in the general population (Bostom et al., 1999; von Eckardstein et al., 1994; Olszewski & Szostak, 1988; Genest et al., 1990; Kang et al., 1991; Robinson et al., 1995; Aronow & Ahn, 1997; Verhoef et al., 1996; Malinow et al., 1997; Christensen et al., 1997; Schwartz et al., 1997; Wu et al., 1994; Malinow et al, 1996; Loehrer et al., 1996; Kang et al., 1986; Ubbink et al., 1991; Montalescot et al., 1997; Dalery et al., 1995; Pancharuniti et al., 1994; Graham et al., 1997; Kluijtmans et al., 1996; Lolin et al., 1996; Verhoef et al., 1997; Israelsson, Brattstrom, & Hultberg, 1988; Clarke et al., 1991; Wilcken & Wilcken, 1976; Murphy-Chutorian et al., 1985; Wald et al., 1998; Stampfer et al., 1992; Arnesen et al., 1995; Bots et al., 1999) [C, II-2].
- There is insufficient evidence to recommend for or against screening for hyperhomocysteinemia in high-risk populations (Ubbink et al., 1998; Stehouwer et al., 1998; Bostom et al., 1999; Nygard et al., 1997; Taylor et al., 1999; von Eckardstein et al., 1994; Olszewski & Szostak, 1988; Genest et al., 1990; Kang et al., 1991; Robinson et al., 1995; Aronow & Ahn, 1997; Verhoef et al., 1996; Malinow et al., 1997; Christensen et al., 1997; Schwartz et al., 1997; Wu et al., 1994; Malinow et al., 1996; Loehrer et al., 1996; Kang et al., 1986; Ubbink et al., 1991; Montalescot et al., 1997; Dalery et al., 1995; Pancharuniti et al., 1994; Graham et al., 1997; Kluijtmans et al., 1996; Lolin et al., 1996; Verhoef et al., 1997; Israelsson, Brattstrom, & Hultberg, 1988; Clarke et al., 1991; Wilcken & Wilcken, 1976; Murphy-Chutorian et al., 1985; Stampfer et al., 1992; Bots et al., 1999) (C, II-2), however, screening may identify individuals at higher risk of developing coronary artery disease, leading to aggressive risk factor modification.
- There is insufficient evidence to recommend for or against treatment of hyperhomocysteinemia with vitamin therapy (Homocysteine Lowering Trialists' Collaboration, 1998; Cuskelly et al., 1995; Schorah et al., 1998; Jacques et al., 1999; Malinow et al., 1998; Rimm et al., 1998; Guttormsen et al., 1996; Ward et al., 1997; Jacob et al., 1994; Franken, Boers, Blom, & Trijbels, 1994; Franken, Boers, Blom, Trijbels, & Kloppenborg, 1994; Van den Berg et al., 1994; Peterson & Spence, 1998) (C, II-1, II-2, II-3).

Definitions:

Recommendation Grades:

A. Good evidence to support the recommendation that the condition or maneuver be specifically considered in a periodic health examination (PHE).
B. Fair evidence to support the recommendation that the condition or maneuver be specifically considered in a PHE.
C. Poor evidence regarding inclusion or exclusion of the condition or maneuver in a PHE, but recommendations may be made on other grounds.
D. Fair evidence to support the recommendation that the condition or maneuver be specifically excluded from consideration in a PHE.
E. Good evidence to support the recommendation that the condition or maneuver be specifically excluded from consideration in a PHE.

Levels of Evidence:

I - Evidence from at least 1 properly randomized controlled trial (RCT).

II-1 - Evidence from well-designed controlled trials without randomization.

II-2 - Evidence from well-designed cohort or case-control analytic studies, preferably from more than 1 centre or research group.

II-3 - Evidence from comparisons between times or places with or without the intervention. Dramatic results in uncontrolled experiments could also be included here.

III - Opinions of respected authorities, based on clinical experience, descriptive studies or reports of expert committees.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

REFERENCES SUPPORTING THE RECOMMENDATIONS

References open in a new window

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

Maneuver: Screening for plasma total homocysteine level in the general population.
Level of Evidence:
One cohort and 30 case-control studies (II-2)

Maneuver: Screening for plasma total homocysteine level in people at high risk for coronary artery disease events.
Level of Evidence:
Five cohort and 28 case-control studies (II-2)

Maneuver: Vitamin therapy
Level of Evidence:
Five randomized controlled trials (I)
One cohort study (II-2)
Seven uncontrolled studies (II-3)

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Cardiovascular disease is the leading cause of death in Canada. Homocysteine, generated in the metabolism of methionine, may have a role in the development of cardiovascular disease. The prevalence of hyperhomocysteinemia in the general population is between 5% and 10% and may be as high as 30%–40% in the elderly population. If population-based studies are correct, total homocysteine may be responsible for up to 10% of coronary artery disease events and thus may represent an important and potentially modifiable risk factor for cardiovascular disease

POTENTIAL HARMS

High-pressure liquid chromatography, the most common method used to measure total homocysteine, has a coefficient of variation of 3 to 11%. Total homocysteine levels may be falsely lowered in the acute phase of illness, such as myocardial infarction, while factors that may elevate total homocysteine include genetic predisposition, increasing age, male gender, serum creatinine, as well as delays in placing samples on ice. Medications such as anti-epileptic drugs, methotrexate, nitrous oxide, and certain disease states, such as psoriasis, acute lymphoblastic leukemia, breast cancer, and hypothyroidism also increase levels, likely through effects on vitamin status. Homocysteine is inversely correlated with serum vitamin B_6, B_{12}, and folate. Thus, in populations with a higher prevalence of B_{12} deficiency (such as the elderly), the specificity of plasma total homocysteine as a cardiac risk factor may be reduced.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

Implementation of preventive activities in clinical practice continues to be a challenge. To address this issue, Health Canada established a National Coalition of Health Professional Organizations in 1989. The purpose was to develop a strategy to enhance the preventive practices of health professionals. Two national workshops were held. The first focused on strengthening the provision of preventive services by Canadian physicians. The second addressed the need for collaboration among all health professionals. This process led to the development of a framework or "blueprint for action" for strengthening the delivery of preventive services in Canada (Supply and Services Canada: an Inventory of Quality Initiatives in Canada: Towards Quality and Effectiveness. Health and Welfare Canada, Ottawa, 1993). It is a milestone for professional associations and one that will have a major impact on the development of preventive policies in this country.

In 1991 the Canadian Medical Association spearheaded the creation of a National Partnership for Quality in Health to coordinate the development and implementation of practice guidelines in Canada. This partnership includes the following: the Association of Canadian Medical Colleges, the College of Family Physicians of Canada, the Federation of Medical Licensing Authorities of Canada, the Royal College of Physicians and Surgeons of Canada, the Canadian Council on Health Facilities Accreditation, and the Canadian Medical Association.

The existence of guidelines is no guarantee they will be used. The dissemination and diffusion of guidelines is a critical task and requires innovative approaches and concerted effort on the part of professional associations and health care professionals. Continuing education is one avenue for the dissemination of guidelines. Local physician leaders, educational outreach programs, and computerized reminder systems may complement more traditional methods such as lectures and written materials.

Public education programs should also support the process of guideline dissemination. In this context, rapidly expanding information technology, such as interactive video or computerized information systems with telephone voice output, presents opportunities for innovative patient education. The media may also be allies in the communication of some relevant aspects of guidelines to the public. All of these technologies should be evaluated.

The implementation of multiple strategies for promoting the use of practice guidelines requires marshaling the efforts of governments, administrators, and health professionals at national, provincial and local levels. It is up to physicians and other health professionals to adopt approaches for the implementation of guidelines in clinical practice and to support research efforts in this direction.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness
Staying Healthy

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

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ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2000

GUIDELINE DEVELOPER(S)

Canadian Task Force on Preventive Health Care - National Government Agency [Non-U.S.]

SOURCE(S) OF FUNDING

The Canadian Task Force on Preventive Health Care is funded through a partnership between the Provincial and Territorial Ministries of Health and Health Canada.

GUIDELINE COMMITTEE

Canadian Task Force on Preventive Health Care (CTFPHC)

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

A complete list of planned reviews, updates and revisions is available under the What's New section at the CTFPHC Web site.

GUIDELINE AVAILABILITY

Electronic copies: Available from the Canadian Task Force on Preventive Health Care (CTFPHC) Web site.

Also available from the from the Canadian Medical Association Journal (CMAJ) Web site in HTML and Portable Document Format (PDF).

Print copies: Available from Canadian Task Force on Preventive Health Care, 100 Collip Circle, Suite 117, London, Ontario N6G 4X8, Canada.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- Stachenko S. Preventive guidelines: their role in clinical prevention and health promotion. Ottawa: Health Canada, 1994. Available from the Canadian Task Force on Preventive Health Care (CTFPHC) Web site.
- CTFPHC history/methodology. Ottawa: Health Canada, 1997. Available from the CTFPHC Web site.
- Quick tables of current recommendations. Ottawa: Health Canada, 2000. Available from the CTFPHC Web site.

PATIENT RESOURCES

None available

NGC STATUS

This summary was completed by ECRI on March 24, 2001. The information was verified by the guideline developer as of June 1, 2001.

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